

In the Claims

Please (first) amend claim 1 as shown in the attached complete set of pending claims as amended.

A complete set of the claims, as amended, in plain text form is also attached.

Remarks

1. Objections to the Specification

The specification is objected to at page 2.

A sentence fragment is deleted by amendment.

2. Rejections of the Claims

Claims 1, 2 and 4-6 are rejected under 35 U.S.C. section 102 over the prior art reference of Sammak, et al.

Claim 7 is rejected 35 U.S.C. section 103 over the prior art reference of Sammak, et al. in vies of Polak, et al.

Claims 3 and 8-10 are objected to, but stated to be allowable if redrafted in independent form.

Claims 11-13 are allowed.

Rather than redrafting claims 3 and/or 8-10 to be of independent form, Applicant amends claim 1.

2.1 The Reference Art

Applicant full well understands that he must distinguish his invention as claimed over the reference art. Before so doing, Applicant begs the indulgence of the Examiner for the following six paragraphs of commentary on the reference art.

Sammak, et al. describe that micro beads have fluorescent spectra and can be mixed for to get a two or more color response. Sammak uses this response to calibrate his optical apparatus.

This approach differs from Applicant in several areas. Applicant is **not** concerned with calibration of the optical apparatus, only that the apparatus should permit the showing of a fluorescent step wedge, or standard (which normally is calibrated), within the same image in which a (normally macroscopic image) is also shown. Sammak, et al. calibrate the apparatus; Applicant calibrates the image.

Applicant is looking for a plurality of differing brightness fluorescent responses over an area - whether it be the area of a specimen, such as a mouse with tumors, or the area of Applicant's step wedge. These differing responses could be a function of concentration of the micro beads, or of a coating (Applicant uses nickel chrome in one version of his step wedge), located between the micro beads and the sensor/camera.

Sammak, et al., are using micro beads for a micro response. They place the micro beads in a well or layer, but they are not in any ordered concentrations over an area to get a change in response (brightness). In that last part of paragraph 0046 Sammak, et al., outline a polymeric layer with a fluorescent concentration standard for intensity calibration. The key word is "standard"; in Applicant's invention it would be standards in known steps of brightness or intensity that could be imaged in one image at a macro, and not micro, scale.

The surface outlined by Sammak, et al., are the bottom of a plate i.e., well plate 96. This surface is not imaged but provides point measurements read by a plate reader. Applicant is not using a plate but, as his "step wedge", a macroscopic object the size of a microscope slide where the whole slide is imaged at once and the ordered change in intensity across that slide is what is used for calibration.

A combination of the prior art references of Polak, et al., and of Sammak, et al., are used to reject claim 7. Polak, et al. are using a calibration reference with a ratio to the collected

signal for a ratio to get better signal to noise. They are using Q dots as a reference. Applicant also uses Q dots as a reference but within a multi-stepped reference, that is, a reference showing multiple, stepped, Quantum dot concentrations over an area. Polak, et al., and Sammak, et al., change the concentration of fluorescent emitters over an area, and as such change the intensity of the fluorescent emissions as a function of location. The change in size of the Q dot to change the emission/intensity could work for a microscope application but would not have the same effect for a macroscopic imaging application.

## 2.2 Distinction of Applicant's Invention as Claimed

Applicant amends his claim 1 to specify that:

"... when the body is illuminated and imaged in a same image field and along with a macroscopic specimen also exhibiting fluorescence at multiple areas and intensities then the body serves as an image calibration step web, or gauge, where any of intensities, colors, dimension, overall brightness, and color temperature of any and all of the multiple specimen fluorescent areas may be determined to be properly so imaged, meaning that the each and all specimen areas are imaged so as to show other than black, or no image, but less than saturation...."

Accordingly;

"wherein, by comparison to the body that is within a same image, illumination of the specimen may be adjusted so that the full range of all its fluorescent emissions, dim to bright, are captured within a single image."

Applicant's claimed body, and its function, is quite simple. Any experimentalist can make an image that is saturated, with selected items that are really fluorescing at different intensities all showing saturation fluorescence, or maximum brightness. Likewise, any experimentalist can make an image that is underexposed, with regions that are actually fluorescing, and even differently fluorescing, all appearing dark. The

observational goal is, or course, to show the entire intensity range of the specimen fluorescent emissions in a single image. It is only important that (1) all the emission levels show in the same image, and, if desired or required, (2) some comparison to some imaging standard may be made. This Applicant's claimed "element for calibrating fluorescent light emissions", or 'step wedge' provides.

### 3. Summary

The present amendment and remarks have overcome and discussed each of the bases for the rejections presented in the Office Action. No new subject matter has been introduced by the present amendment.

In consideration of the preceding amendment and accompanying remarks, the present amendment is deemed worthy of entrance, and the present application is deemed in condition for allowance. The timely action of the Examiner to that end is earnestly solicited.

Applicants' undersigned attorney is at the Examiner's disposal should the Examiner wish to discuss any matter which might expedite prosecution of this case.

Sincerely yours,



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CERTIFICATE OF MAILING

I hereby certify that this AMENDMENT and the documents referred to as attached therein are being deposited with the United States Postal Service as first class mail postage prepaid addressed to the: Mail Stop Amendment - Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date written below.

September 25, 2005

Date

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CLAIMS (AS AMENDED)

1. (Currently Amended) An element for calibrating fluorescent light emissions comprising:

a body having a plurality of regions suitably simultaneously illuminated that, under illumination sufficient to induce fluorescence, so as to fluoresce at a corresponding plurality of fluorescent light emission intensities, certain regions appearing to fluoresce relatively more brightly while other regions appear to fluoresce relatively less brightly;

wherein when the body is illuminated and imaged in a same image field and along with a macroscopic specimen also exhibiting fluorescence at multiple areas and intensities then the body serves as an image calibration step web, or gauge, where any of intensities, colors, dimension, overall brightness, and color temperature of any and all of the multiple specimen fluorescent areas may be determined to be properly so imaged, meaning that the each and all specimen areas are imaged so as to show other than black, or no image, but less than saturation;

wherein, by comparison to the body that is within a same image, illumination of the specimen may be adjusted so that the full range of all its fluorescent emissions, dim to bright, are captured within a single image.

2. (Original) The fluorescent light emissions calibration element according to claim 1 wherein the body comprises:

a substantially planar substrate; and  
at least one fluorescent substance within the substrate; and  
one or more coatings applied to different effect in the plurality of areas of the substrate so that the different ones of these plurality of substrate regions will, upon exposure to radiation sufficient to induce fluorescent emissions of the fluorescent substance, appear to fluoresce relatively more brightly while other regions will appear to fluoresce relatively less brightly.

3. (Original) The fluorescent light emissions calibration element according to claim  
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wherein the same coating is applied at various thickness to different ones of the plurality of areas of the fluorescent-substance-containing substrate so that relatively less thickly coated regions of the fluorescent-substance-containing substrate will, upon exposure to radiation sufficient to induce fluorescent emissions of the fluorescent substance, appear to fluoresce relatively more brightly while relatively more thickly coated regions of the fluorescent-substance-containing substrate will, upon exposure to the same radiation sufficient to induce fluorescent emissions of the fluorescent substance, appear to fluoresce relatively less brightly.

4. (Original) The fluorescent light emissions calibration element according to claim  
2 wherein the substantially planar substrate comprises:

glass.

5. (Original) The fluorescent light emissions calibration element according to claim  
2 wherein the substantially planar substrate comprises:

plastic.

6. (Original) The fluorescent light emissions calibration element according to claim  
2 wherein the fluorescent substance comprises:

a fluorescent chemical.

7. (Original) The fluorescent light emissions calibration element according to claim  
2 wherein the fluorescent substance comprises:

quantum dots.

8. (Original) The fluorescent light emissions calibration element according to claim  
2 wherein at least one coating comprises:

nickel chrome.

9. (Original) The fluorescent light emissions calibration element according to claim

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wherein at least one coating is so applied in various regions to the substrate at the variable extent by dint of being applied to the substrate in multiple regions at a first time, and to be re-applied to less than all of the multiple regions upon at least one more, second, time;

wherein the at least one coating is more abundant in those of the multiple regions whereat it has been applied at least two times than any regions whereat it has been applied but one time.

10. (Original) The fluorescent light emissions calibration element according to claim

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wherein the at least one coating is so applied in various regions to the substrate at the variable extent by dint of being applied and re-applied to the substrate in each of multiple regions for a variable number of times;

wherein accumulations of the coating will be greatest in those regions of the substrate whereat the coating has been applied multiple times.

11. (Original) An apparatus for illuminating a macroscopically-sized specimen for

observation along a viewing axis, the apparatus comprising:

a stage for supporting a specimen to be observed; a first illumination source of first radiation of a first color; a second illumination source of second radiation of a second color, different from the first color;

an element for calibrating fluorescent light emissions induced by each of the first and the second radiations, the element having

a body having a plurality of regions that fluoresce under illumination to a corresponding plurality of fluorescent light emission intensities, certain regions appearing to fluoresce relatively more brightly while other regions appear to fluoresce relatively less brightly,

12. (Original) The apparatus according to claim 11 further comprising:

a first sensor sensing induced fluorescent radiation emission from a region of the element that is responsive to the first radiation to fluoresce so as to produce a first signal; and

a first control circuit, responsive to the first signal, for controlling the first radiation output of the radiation source so that this radiation output is relatively greater when the induced fluorescent radiation emission of the element is sensed by the first sensor to be relatively less, and is relatively lesser when the induced fluorescent radiation emission of element is sensed by the first sensor to be relatively greater.

13. (Original) The apparatus according to claim 12 further comprising:

a second sensor sensing induced fluorescent radiation emission from a region of the element that is responsive to the second radiation to fluoresce so as to produce a second signal; and

a second control circuit, responsive to the second signal, for controlling the second radiation output of the radiation source so that this radiation output is relatively greater when the induced fluorescent radiation emission of the element is sensed by the second sensor to be relatively less, and is relatively lesser when the induced fluorescent radiation emission of element is sensed by the second sensor to be relatively greater.



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Illuminations are potentially along each of multiple viewing axis at a single time, and each such illumination of the specimen along each such axis may be in, potentially, multiple colors (i.e., wavelengths, or frequencies) as serve to excite corresponding fluorescent emissions in the specimen in each of multiple colors (i.e., wavelengths, or frequencies). Moreover, each of the potentially plural induced fluorescent emissions (along each illumination and viewing axis) may be independently controlled in intensity. In particular, multiple fluorescing colored fields as appear within a composite, panoramic, image of the specimen may be--by the adjustability of the fluorescent emissions--both (1) made clearly visible, and (2) balanced one color and area of fluorescent emission to the next--meaning that a bright field of one fluorescent color will not "swamp" a dimmer fluorescent field of another color. Moreover, and nonetheless that the induced fluorescent emissions may be adjusted in intensity--meaning that the dim may be made bright simultaneously that the bright may be made dim--the true and actual intensity of each fluorescent emission may be quantitatively known.

~~Nonetheless to all these variables of illumination, the fluorescent~~

The present invention will be seen to still further concern that all such variable illumination along each of multiple axis as produces multi-color fluorescent emissions of controlled intensity (along each axis, as are individually visible in a composite image) is efficiently realized.

Accordingly, whereas (1) a first related invention regarding panoramic viewing may be simplistically regarded as showing how to comprehensively illuminate and view a macroscopic specimen along a single axis at a single time, and (2) a second invention regarding a fluorescent image calibration step wedge may be simplistically regarded as showing how to quantify each of multiply-colored fluorescent emissions permissively simultaneously appearing in each of multiple (illumination and) viewing axis in a composite,